

[Supplementary online-only material for Fiest KM, Fisk JD, Patten SB, et al: Fatigue and comorbidities in multiple sclerosis. *Int J MS Care*. 2016;18(2):96–104.]

**Supplementary Table 1. Participants reporting fatigue at each visit by the presence of baseline comorbid conditions**

Comorbidity	Participants reporting fatigue, <sup>a</sup> % (95% CI)		
	Baseline	Year 1	Year 2
Lupus	88.9 (46.8-98.6) <sup>b</sup>	71.4 (29.8-93.6)	80.0 (25.6-97.9)
Fibromyalgia	82.4 (65.6-92.0) <sup>c</sup>	83.4 (66.2-93.2) <sup>c</sup>	71.9 (53.8-84.8) <sup>b</sup>
Peripheral vascular disease	78.6 (49.3-93.3)	58.3 (29.7-82.3)	60.0 (34.0-81.4)
Glaucoma	78.6 (49.3-93.3)	54.5 (25.7-80.7)	75.0 (43.3-92.2)
IBD	77.8 (52.7-91.7) <sup>b</sup>	76.5 (50.5-91.2) <sup>b</sup>	80.0 (51.9-93.7) <sup>b</sup>
Depression	77.7 (72.4-82.3) <sup>c</sup>	71.8 (66.0-76.9) <sup>c</sup>	68.3 (62.2-73.7) <sup>c</sup>
Anxiety	75.9 (66.9-83.1) <sup>c</sup>	66.0 (56.1-74.6) <sup>c</sup>	70.3 (61.1-78.1) <sup>c</sup>
Cataracts	71.4 (55.9-83.1) <sup>b</sup>	59.5 (44.1-73.3)	61.5 (47.6-73.8)

Rheumatoid arthritis	71.4 (54.3-84.0) <sup>b</sup>	56.7 (38.5-73.2)	70.4 (50.6-84.7)
Diabetes	68.4 (52.0-81.3)	63.4 (47.6-76.8)	69.2 (53.0-81.8) <sup>b</sup>
COPD	67.7 (57.5-76.5) <sup>b</sup>	68.0 (58.1-76.6) <sup>c</sup>	61.6 (50.9-71.3)
IBS	66.2 (54.7-76.1)	61.6 (50.0-72.1)	74.3 (62.7-83.2) <sup>c</sup>
Thyroid disease	66.2 (54.7-76.1)	51.9 (40.8-62.9)	60.2 (49.3-70.2)
Seizure disorder	63.6 (32.5-86.4)	63.6 (32.5-86.4)	75.0 (48.2-90.6)
Migraine	63.4 (55.7-70.5) <sup>b</sup>	70.3 (62.1-77.3) <sup>c</sup>	59.6 (51.1-67.5)
Bipolar disorder	61.5 (33.3-83.7)	57.1 (30.7-80.0)	58.3 (29.7-82.3)
Osteoporosis	61.4 (48.1-73.2)	63.9 (51.1-75.0)	63.3 (50.4-74.6)
Heart disease	60.7 (41.6-77.0)	58.1 (40.1-74.1)	55.9 (38.9-71.6)
Hypertension	60.1 (52.5-67.3)	58.2 (50.9-65.1)	59.7 (52.2-66.7)
Hypercholesterolemia	59.3	56.0	55.7

	(50.2-67.8)	(47.2-64.5)	(46.8-64.3)
No comorbidity	53.8 (50.6-56.9)	51.3 (48.1-55.6)	51.4 (48.1-54.7)

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome.

<sup>a</sup>According to the any fatigue definition (Fatigue Impact Scale for Daily Use score  $\geq 5$  vs.  $< 5$ ).

<sup>b</sup> $P < .05$  compared with no comorbidity.

<sup>c</sup> $P < .01$  compared with no comorbidity.

**Supplementary Table 2. Ordinal generalized estimating equation model of fatigue in four groups over time**

<b>Condition</b>	<b>OR (95% CI)<sup>a</sup></b>	<b>Exact <i>P</i> value</b>	<b>OR adjusted for depressive symptoms</b>	<b>Exact <i>P</i> value</b>	<b>Comorbidity × time interaction <i>P</i> value</b>
Any comorbidity	1.65 (1.24-2.18) <sup>b</sup>	.0005	1.67 (1.22-2.29) <sup>b</sup>	.0014	.99
Depression	2.58 (2.03-3.27) <sup>b</sup>	<.0001	2.10 (1.54-2.87) <sup>bc</sup>	<.0001	.34
IBS	1.71 (1.18-2.48) <sup>b</sup>	.004	1.39 (0.85-2.29)	.19	.23
Migraine	1.69 (1.27-2.27) <sup>b</sup>	.0004	1.51 (1.08-2.13) <sup>b</sup>	.02	.61
Anxiety	1.57 (1.15-2.16) <sup>b</sup>	.005	1.27 (0.84-1.91)	.26	.72
COPD	1.37 (0.98-1.92)	.06	1.25 (0.78-2.00)	.35	.81
Hypertension	1.25 (0.95-1.65)	.11	1.11 (0.79-1.57)	.55	.43
Thyroid disease	1.23 (0.85-1.78)	.28	1.30 (0.84-2.01)	.24	.76
Hypercholesterolemia	0.92	.59	0.83	.38	.88

	(0.67-1.25)		(0.56-1.25)		
Osteoporosis	0.80 (0.52-1.24)	.32	0.80 (0.48-1.35)	.41	.76

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; OR, odds ratio.

<sup>a</sup>Adjusted for visit time (continuous), time since symptom onset (years), disability status (Expanded Disability Status Scale score), age, sex, educational level, and the presence of other comorbidities (depression, hypertension, migraine, hypercholesterolemia, anxiety, COPD, IBS, autoimmune thyroid disease, and osteoporosis).

<sup>b</sup>Significant at  $\alpha = 0.05$ .

<sup>c</sup>Adjusted for the above variables but only current depressive symptoms (instead of the history/current variable, since this is included).

**Supplementary Table 3. Models of change scores with logistic generalized estimating equation of worsening fatigue**

Condition	OR (95% CI) <sup>a</sup>	Exact <i>P</i> value
Depression	1.49 (1.08-2.07) <sup>b</sup>	.02
COPD	1.14 (0.75-1.75)	.54
Osteoporosis	1.07 (0.60-1.92)	.81
Migraine	1.01 (0.70-1.46)	.95
Thyroid disease	1.00 (0.63-1.58)	.99
Hypertension	0.93 (0.65-1.34)	.70
IBS	0.90 (0.55-1.47)	.68
Hypercholesterolemia	0.85 (0.57-1.26)	.41
Anxiety	0.83 (0.53-1.31)	.42

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; IBS, irritable bowel syndrome; OR, odds ratio.

<sup>a</sup>Adjusted for visit time (continuous), time since symptom onset (years), disability status (Expanded Disability Status Scale score), age, sex, educational level, and the presence of individual comorbidities (hypercholesterolemia, migraine, COPD, IBS, autoimmune thyroid disease, hypertension, osteoporosis, depression, and anxiety).

<sup>b</sup>Significant at  $\alpha = 0.05$ .

**Supplementary Table 4. Models of change scores with logistic generalized estimating equation of worsening fatigue (same/better vs. worse) in those with/without active symptoms or a history of depression**

<b>Condition</b>	<b>Odds ratio<sup>a</sup> with depressive symptoms<sup>b</sup></b>	<b>Exact <i>P</i> value</b>
Depression	1.40 (1.01-1.95) <sup>c</sup>	.04
COPD	1.12 (0.72-1.72)	.62
Osteoporosis	1.07 (0.61-1.89)	.81
Any comorbidity <sup>d</sup>	1.14 (0.76-1.72)	.52
Thyroid disease	1.00 (0.63-1.59)	.99
Migraine	0.97 (0.67-1.40)	.87
Hypertension	0.90 (0.62-1.30)	.57
IBS	0.90 (0.55-1.47)	.67
Hypercholesterolemia	0.84 (0.57-1.25)	.39
Anxiety	0.80 (0.50-1.26)	.34

Abbreviations: COPD, chronic obstructive pulmonary disease; IBS, irritable bowel syndrome.

<sup>a</sup>Adjusted for visit time (continuous), time since symptom onset (years), disability status (Expanded Disability Status Scale score), age, sex, educational level, and the presence of comorbidities (hypercholesterolemia, migraine, COPD, IBS, autoimmune thyroid disease, hypertension, osteoporosis, depression, and anxiety).

<sup>b</sup>Categorized into four groups: no current depressive symptoms, no history of depression; current depressive symptoms, no history of depression; no current depressive symptoms, a history of

depression; both current symptoms and a history of depression. The depression variable was adjusted only for the presence of current symptoms.

<sup>c</sup>Significant at  $\alpha = 0.05$ .

<sup>d</sup>Not adjusted for the presence of comorbidities but for all the other aforementioned variables.